

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 April 2001 (05.04.2001)

PCT

(10) International Publication Number
WO 01/22920 A2

(51) International Patent Classification⁷: **A61K**

(21) International Application Number: **PCT/US00/26524**

(22) International Filing Date:
28 September 2000 (28.09.2000)

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
60/157,137 29 September 1999 (29.09.1999) **US**
60/163,280 3 November 1999 (03.11.1999) **US**

(71) Applicant (for all designated States except US): **HUMAN GENOME SCIENCES, INC.** [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **RUBEN, Steven, M.** [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). **BARASH, Steven, C.** [US/US]; 111 Watkins Pond Blvd., #301, Rockville, MD 20850 (US). **BIRSE, Charles, E.** [GB/US]; 13822 Saddleview Drive, North Potomac, MD 20878 (US). **ROSEN, Craig, A.** [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US).

(74) Agents: **HOOVER, Kenley, K.** et al.; c/o Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).

(81) Designated States (national): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.**

(84) Designated States (regional): **ARIPO** patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), **Eurasian** patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), **European** patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), **OAPI** patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— Without international search report and to be republished upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **COLON AND COLON CANCER ASSOCIATED POLYNUCLEOTIDES AND POLYPEPTIDES**

(57) Abstract: This invention relates to newly identified colon or colon cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "colon cancer antigens", and the use of such colon cancer antigens for targeting specific cell types and/or diagnosing, detecting, preventing and treating disorders of the colon, particularly the presence of colon cancer and colon cancer metastases. This invention relates to colon cancer antigens as well as vectors, host cells, antibodies directed to colon cancer antigens and the recombinant or synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to the colon, including colon cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of colon cancer antigens of the invention. The present invention further relates to inhibiting the production and function of the polypeptides of the present invention.

WO 01/22920 A2

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X which is hybridizable to SEQ ID NO:X;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y which is hybridizable to SEQ ID NO:X;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y which is hybridizable to SEQ ID NO:X, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:X;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y, which is hybridizable to SEQ ID NO:X.

2225

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X, which is hybridizable to SEQ ID NO:X.
5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
9. A recombinant host cell produced by the method of claim 8.
10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polypeptide fragment of SEQ ID NO:Y;
 - (b) a polypeptide fragment of SEQ ID NO:Y, having biological activity;
 - (c) a polypeptide domain of SEQ ID NO:Y;
 - (d) a polypeptide epitope of SEQ ID NO:Y;
 - (e) a full length protein of SEQ ID NO:Y;
 - (f) a variant of SEQ ID NO:Y;
 - (g) an allelic variant of SEQ ID NO:Y; or
 - (h) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

2227

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

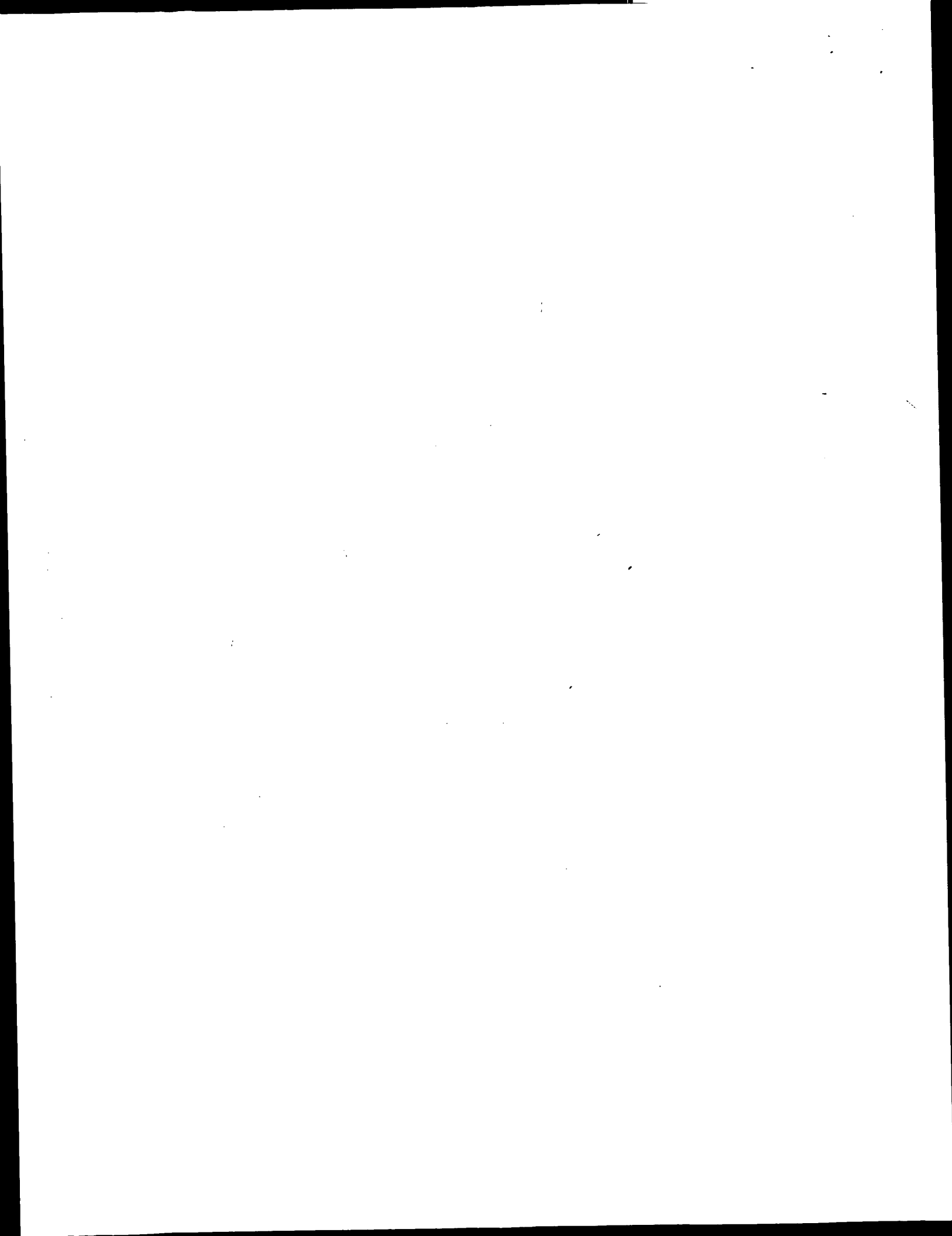
(a) expressing SEQ ID NO:X in a cell;

(b) isolating the supernatant;

(c) detecting an activity in a biological assay; and

(d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.



1219

```

tgggaacagc agagatgaat ggcaaaactca tagctgcagg tggctataac agagaggaat 780
gtcttcgaac agtcgaatgc tataatccac atacagatca ctggtccttt cttgctccca 840
tgagaacacc aagagcccgga tttcaaattg ctgtactcat gggccagctc tatgtggttag 900
gtggatcaaa tggccactca gatgacctga gttgtggaga gatgtatgat tcaaacatag 960
atgactggat tcctgttcca gaattgagaa ctaaccgttg taatgcagga gtgtgtgctc 1020
tgaatggaaa gttatacatc gttgtgtggct ctgatccata tggtaaaaaa ggactgaaaa 1080
attgtgatgt atttgatcct gtaacaaagt tgtggacaag ctgtgccccct cttaacattc 1140
ggagacacca gtctgcagtc tgtgagcttg gtggttattt gtacataatc ggaggtgcag 1200
aatcttgga ttgtctgaac acagtagaac gatacaatcc tgaataaat acctggactt 1260
taattgcacc catgaatgtg gctaggcgag gagctggagt ggctgttctt aatggaaaaac 1320
tgtttgtatg tgggtggcttt gatgggttctc atgccatcag ttgtgtggaa atgtatgatc 1380
caactagaaa tgaatggaag atgatgggaa atatgacttc accaaggagc aatgctggga 1440
ttgcaactgt agggaaacacc atttatgcag tgggaggatt cgatggcaat gaatttctga 1500
atacgggtgga agtctataac cttgagtcaa atgaatggag cccctataca aagattttcc 1560
agttttaaca aatttaagac cctctcaaac taacaggctt agtgatgtaa ttatgggttag 1620
yagaggtaca cttgtgaata aagagggttg gtgggtatag atgttgctaa cagcaacaca 1680
aagcttttgc atattgcata ctattaaaca tctgtacat actttttggg tttatttgga 1740
aaggaatgca aagatgaagg tctgttttgt gtacttttaa gactttggtt attttacttt 1800
ttggaaaaaga ataaaccaag aattgatttg gcacatcaaa aaaaaaaaaa aaaaaaaaaa 1860
aaaagggcgg ccgctcaaga gtat

```

1884

<210> 1941

<211> 2731

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (42)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (50)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1629)

<223> n equals a,t,g, or c

<400> 1941

```

aaggcgtctg gagtttaatg ttacttgggtg atatgagact tncattcttn cagggtggaag 60
atgagctcag ctccccagtg gtgggtgttca gatttttcca ggaattacca ggctcagatc 120
cgggtgtttaa agccgtccca gtgcccacaa tgacaccttc aggagtcggc cgggagagggc 180
actcgtgtga cgcgtgaat cgctggctgg gagaacagct gaagcagctg gtgcctgcaa 240
gcggcctcac agtcatggat ctggaagctg agggcacgtg tttgcggttc agccctttga 300
tgaccgcagc agtttttagga actcggggag aggatgtgga tcagctcgta gcctgcatag 360
aaagcaaaact gccagtgtctg tgctgtacgc tccagttgcy tgaagagttc aagcaggaag 420
tggaagcaac agcaggtctc ctatatgttg atgacctaa ctggtctgga ataggggttg 480
tcaggatga acatgctaata gatgataaga gcagtttgaa atcagatccc gaaggggaaa 540

```


305					310					315					320
Asp	Trp	Ile	Pro	Val	Pro	Glu	Leu	Arg	Thr	Asn	Arg	Cys	Asn	Ala	Gly
				325					330					335	
Val	Cys	Ala	Leu	Asn	Gly	Lys	Leu	Tyr	Ile	Val	Gly	Gly	Ser	Asp	Pro
			340					345					350		
Tyr	Gly	Gln	Lys	Gly	Leu	Lys	Asn	Cys	Asp	Val	Phe	Asp	Pro	Val	Thr
		355					360					365			
Lys	Leu	Trp	Thr	Ser	Cys	Ala	Pro	Leu	Asn	Ile	Arg	Arg	His	Gln	Ser
	370					375					380				
Ala	Val	Cys	Glu	Leu	Gly	Gly	Tyr	Leu	Tyr	Ile	Ile	Gly	Gly	Ala	Glu
385					390					395					400
Ser	Trp	Asn	Cys	Leu	Asn	Thr	Val	Glu	Arg	Tyr	Asn	Pro	Glu	Asn	Asn
				405					410					415	
Thr	Trp	Thr	Leu	Ile	Ala	Pro	Met	Asn	Val	Ala	Arg	Arg	Gly	Ala	Gly
			420					425					430		
Val	Ala	Val	Leu	Asn	Gly	Lys	Leu	Phe	Val	Cys	Gly	Gly	Phe	Asp	Gly
		435					440					445			
Ser	His	Ala	Ile	Ser	Cys	Val	Glu	Met	Tyr	Asp	Pro	Thr	Arg	Asn	Glu
	450					455					460				
Trp	Lys	Met	Met	Gly	Asn	Met	Thr	Ser	Pro	Arg	Ser	Asn	Ala	Gly	Ile
465					470					475					480
Ala	Thr	Val	Gly	Asn	Thr	Ile	Tyr	Ala	Val	Gly	Gly	Phe	Asp	Gly	Asn
				485					490					495	
Glu	Phe	Leu	Asn	Thr	Val	Glu	Val	Tyr	Asn	Leu	Glu	Ser	Asn	Glu	Trp
			500					505					510		
Ser	Pro	Tyr	Thr	Lys	Ile	Phe	Gln	Phe							
		515					520								

<220>
<221> SITE
<222> (14)

5436

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (16)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 6218

Gly Val Trp Ser Leu Met Leu Leu Gly Asp Met Arg Leu Xaa Phe Xaa
1 5 10 15

Gln Val Glu Asp Glu Leu Ser Ser Pro Val Val Val Phe Arg Phe Phe
20 25 30

Gln Glu Leu Pro Gly Ser Asp Pro Val Phe Lys Ala Val Pro Val Pro
35 40 45

Asn Met Thr Pro Ser Gly Val Gly Arg Glu Arg His Ser Cys Asp Ala
50 55 60

Leu Asn Arg Trp Leu Gly Glu Gln Leu Lys Gln Leu Val Pro Ala Ser
65 70 75 80

Gly Leu Thr Val Met Asp Leu Glu Ala Glu Gly Thr Cys Leu Arg Phe
85 90 95

Ser Pro Leu Met Thr Ala Ala Val Leu Gly Thr Arg Gly Glu Asp Val
100 105 110

Asp Gln Leu Val Ala Cys Ile Glu Ser Lys Leu Pro Val Leu Cys Cys
115 120 125

Thr Leu Gln Leu Arg Glu Glu Phe Lys Gln Glu Val Glu Ala Thr Ala
130 135 140

Gly Leu Leu Tyr Val Asp Asp Pro Asn Trp Ser Gly Ile Gly Val Val
145 150 155 160

Arg Tyr Glu His Ala Asn Asp Asp Lys Ser Ser Leu Lys Ser Asp Pro
165 170 175

Glu Gly Glu Asn Ile His Ala Gly Leu Leu Lys Lys Leu Asn Glu Leu
180 185 190

Glu Ser Asp Leu Thr Phe Lys Ile Gly Pro Glu Tyr Lys Ser Met Lys
195 200 205

Ser Cys Leu Tyr Val Gly Met Ala Ser Asp Asn Val Asp Ala Ala Glu
210 215 220

Leu Val Glu Thr Ile Ala Ala Thr Ala Arg Glu Ile Glu Glu Asn Ser

5437

225		230		235		240
Arg Leu Leu Glu Asn Met Thr Glu Val Val Arg Lys Gly Ile Gln Glu						
	245			250		255
Ala Gln Val Glu Leu Gln Lys Ala Ser Glu Glu Arg Leu Leu Glu Glu						
	260		265			270
Gly Val Leu Arg Gln Ile Pro Val Val Gly Ser Val Leu Asn Trp Phe						
	275		280			285
Ser Pro Val Gln Ala Leu Gln Lys Gly Arg Thr Phe Asn Leu Thr Ala						
	290		295			300
Gly Ser Leu Glu Ser Thr Glu Pro Ile Tyr Val Tyr Lys Ala Gln Gly						
	305		310		315	320
Ala Gly Val Thr Leu Pro Pro Thr Pro Ser Gly Ser Arg Thr Lys Gln						
	325			330		335
Arg Leu Pro Gly Gln Lys Pro Phe Lys Arg Ser Leu Arg Gly Ser Asp						
	340			345		350
Ala Leu Ser Glu Thr Ser Ser Val Ser His Ile Glu Asp Leu Glu Lys						
	355			360		365
Val Glu Arg Leu Ser Ser Gly Pro Glu Gln Ile Thr Leu Glu Ala Ser						
	370		375			380
Ser Thr Glu Gly His Pro Gly Ala Pro Ser Pro Gln His Thr Asp Gln						
	385		390		395	400
Thr Glu Ala Phe Gln Lys Gly Val Pro His Pro Glu Asp Asp His Ser						
	405			410		415
Gln Val Glu Gly Pro Glu Ser Leu Arg						
	420			425		

<210> 6219

<211> 130

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (22)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

